PROTEIN CONFORMATIONAL STABILITY AND INTERACTIONS: THERMODYNAMIC EXPLOITATION OF CALORIMETRIC DATA

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ABSTRACT

Calorimetry is widely used for the characterization of bio-systems. The rather well defined general picture of the field implies the use of techniques and theoretical approaches that depend not only on the chemical peculiarities but mainly on the status of the system with respect to the aqueous medium and the co-solutes.

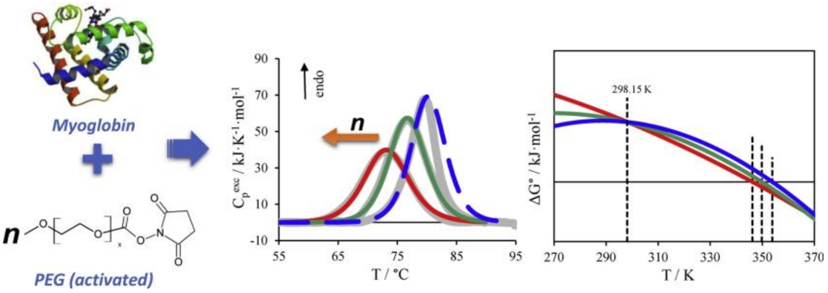

Figure 1: Protein thermodynamic stability evaluated from DSC data (graphical abstract, [1]).

In the frame of biological and pharmaceutical research, particular interest is devoted to the study the thermodynamic properties of globular proteins in diluted solution (mimicking physiological conditions) to be correlated with the structural information (crystallography, MD Simulations, NMR, etc). In this context, calorimetric data, once treated according to the formal expressions of thermodynamics and statistical mechanics, allow evaluation of the partition function of the system which includes all the thermodynamic information about the accessible states and their stability, singling out enthalpic from entropic contributions. More specifically, the HS-DSC (High Sensitive Differential Scanning Calorimetry) provides quantitative information about the mechanisms of the conformational transitions and the thermal stability of the energetic domains of the macromolecules, allowing one to separate the contributions relevant to either the solvent or the co-solutes that are responsible for specific interactions [2-3]. Further details about the thermodynamics of this kind of interaction (affinity constant, interaction enthalpy and entropy, cooperativity, allosteric effects, etc.) can be drawn from ITC (isothermal titration calorimetry) investigations [4,5].

However, despite the principles of equilibrium thermodynamics for these systems are well consolidated, they present a vast range of peculiarities that requires the implementation of specific thermodynamic models for a full experimental data exploitation that are often beyond the approaches offered by the common instrumental software.

In this frame we present some case studies on these biological systems investigated in our laboratory to highlight the methodologic approach for a suitable thermodynamic analysis.

Keywords: Proteins, DSC, ITC, Thermodynamics

Physics and Astronomy Classification Scheme: 87.15.hp, 87.15.kp, 07.20.Fw

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